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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,432	06/13/2006	Nicolas Burdin	06-439	6546

20306 7590 12/10/2009

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EXAMINER	
YOUNG, SHAWQUIA	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
12/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,432	BURDIN ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 are currently pending in the instant application. Applicants have amended claims 1 and 2 in an amendment filed on August 5, 2009. Claims 1-6 are rejected in this Office Action.

I. ***Response to Arguments/Remarks***

Applicants' amendment, filed August 5, 2009 has overcome the objection to claims 1-6 as containing non-elected subject matter. The objection has been withdrawn.

Applicants' arguments relating to the rejection of claims 1-6 under 35 USC 103 as being unpatentable over Hawkins, et al. (US Patent 6,290,973) and Gerster, et al. (US Patent 5,389,640) in view of Janssens, et al. have been fully considered but are partially persuasive. Applicants argue that as demonstrated in the declaration, filed on August 5, 2009, that it was not expected that the combination of the TLR 4 agonist with either the TLR 7 agonist or the TLR 8 agonist would give improved results because it had been found that the combination of the TLR 4 agonist with the TLR agonist did not give improved results.

First, the Examiner wants to point out that Applicants have shown that a combination of the specific compounds ER804057 and R-848 do have a potentiated effect compared to each compounds individual effects and are considered unobvious. However, the Examiner wants to point out that Applicants have not shown that the combination of a specific Toll-like 7 agonist in combination with a Toll-like 4 agonist has

a potentiated effect which is considered unexpected results. In all of the working examples in the instant specification, Applicants have used ER804057, a Toll-like 4 agonists, and R-848, a Toll-like 7 agonist and a Toll-like 8 agonist (see pages 7-14 of the specification). Applicants have not provided any data which specifies which receptor, Toll-like 7 receptor or Toll-like 8 receptor, is actually responsible for the potentiated effect seen when ER804057 and R-848 are combined since R-848 is an agonist for both Toll-like 7 receptor and Toll-like 8 receptor. The potentiatied immunostimulatory effect could be caused by the activation of both Toll-like 4 receptor and Toll-like 7 receptor; the activation of both Toll-like 4 receptor and Toll-like 8 receptor or the activation of all three receptors. Therefore without data specifying which receptor, Toll-like 7, Toll-like 8 or both, is responsible for the potientiated effect seen by the combination of ER804057 and R-848, than it is unclear whether a composition comprising a specific Toll-like 7 receptor agonist and a Toll-like 4 receptor agonist does indeed produce a potentiated effect and is considered unobvious.

Applicants' declaration has been fully considered but has not been found persuasive relating to the 103 rejection. Applicants' declaration relates to the immunostimulatory response of the combination of Toll-like 2 receptor agonist, H8820, and Toll-like 4 receptor agonist, ER804057. However, the instant claims do not relate to a Toll-like 2 receptor and therefore does not overcome the 103 rejection.

The Examiner has maintained the rejection of claims 1-6 under 35 USC 103 as being unpatentable over Hawkins, et al. and Gerster, et al. in view of Janssens, et al.

II. *Rejection(s)*

35 USC § 103 - OBVIOUSNESS REJECTION

The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Graham v. John Deere Co. set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). *See Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Hawkins, et al.* (US Patent 6,290,973) and *Gerster, et al.* (US Patent 5,389,640) in view of *Janssens, et al.* Applicants' claims are drawn to an immunostimulant composition comprising at least one agonist of the Toll-like 7 receptor or of the Toll-like 8 receptor, wherein the composition additionally comprises an agonist of the Toll-like 4 receptor. Applicants have elected the an immunostimulant composition comprising the Toll-like 7

receptor agonist, 4-amino-2-ethoxymethyl-α,α-dimethyl-1-H-imidazo[4,5c]quinoline-1-ethanol and the Toll-like 4 receptor agonist, ER804057.

The Scope and Content of the Prior Art (MPEP §2141.01)

Hawkins, et al. teaches immunological adjuvant compounds such as ER804057 (See column 6, line 45 and table 6, columns 187-188) that can be used in immunostimulatory compositions.

Gerster, et al. teaches 1H-imidazo[4,5-c]quinoline compounds such as 4-amino-2-ethoxymethyl-α,α-dimethyl-1-H-imidazo[4,5c]quinoline-1-ethanol (See columns 35 and 36, examples 99 and 101) which can be used antivirals. The prior art reference further teaches compositions comprising the 1—imidazo[4,5c]quinoline compounds.

The secondary reference, *Janssens, et al.*, teaches the role of toll-like receptors in pathogen recognition. On page 639, the reference teaches that toll-like 7 receptors and toll-like 8 receptors have been shown to recognize synthetic antiviral compounds with strong immunostimulatory capacity belonging to the group of imidazoquinolines.

The Difference Between the Prior Art and the Claims (MPEP §2141.02)

The difference between the prior art of *Hawkins, et al.* and *Gerster, et al.* and the instant invention is that Applicants have formulated an immunostimulant composition comprising of a toll-like 7 receptor agonist, 4-amino-2-ethoxymethyl-α,α-dimethyl-1-H-imidazo[4,5c]quinoline-1-ethanol and a toll-like 4 receptor agonist, ER804057.

Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)

Applicants are claiming an immunostimulant composition comprising at least one

agonist of the Toll-like 7 receptor, wherein the composition additionally comprises an agonist of the Toll-like 4 receptor and have elected the an immunostimulant composition comprising the Toll-like 7 receptor agonist and Toll-like 8 receptor agonist, 4-amino-2-ethoxymethyl-α,α-dimethyl-1-H-imidazo[4,5c]quinoline-1-ethanol and the Toll-like 4 receptor agonist, ER804057. The prior art reference of *Hawkins, et al.* teaches the compound ER804057 and its use in immunostimulatory compositions. The prior art reference *Gerster, et al.* teaches the compound 4-amino-2-ethoxymethyl-α,α-dimethyl-1-H-imidazo[4,5c]quinoline-1-ethanol and its use in compositions as an antiviral. The secondary prior art reference *Janssens, et al.* teaches in general the role of toll-like receptors in pathogen recognition and specifically teaches that the imidazoquinoline class of compounds have strong immunostimulatory capacity which are ligands of Toll-like 7 receptors and Toll-like 8 receptors.

In In re Kerkoven, 626 F.2d 846, 205 USPQ 1069 (CCPA 1980), it was well established that it is obvious to combine individual compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. Specifically, it is obvious to prepare an immunostimulant composition comprising a toll-like 7 agonist and a toll-like 4 agonist when the art teaches that a toll-like agonist can be used in immunostimulant composition and also teaches that a toll-like 7 agonist and Toll-like 8 agonist have strong immunostimulatory capacity with a reasonable expectation of success. Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to prepare an immunostimulant composition comprising a Toll-like 7 receptor

agonist and a Toll-like 4 receptor agonist based on the teachings of the preferred embodiments in the prior art. A strong prima facie obviousness has been established.

III. Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626